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(54) Title: COMBINATION THERAPY USING COX-2 SELECTIVE INHIBITOR AND THROMBOXANE INHIBITOR AND COMPOSITIONS THEREFOR

(57) Abstract: The present invention provides a method for the treatment or prophylaxis of COX-2 mediated conditions in patients who are at risk of developing thromboembolic events which comprises administering to said patient a therapeutically or prophylactically effective amount of a COX-2 selective inhibitor and a cardiovascular protective amount of a thromboxane inhibitor, as well as compositions therefor.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 01/00683

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K45/06 A61P35/00 A61P25/28 A61P19/02 A61P9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 50033 A (LUNDY KRISTIN MARIE ; RICKETTS ANTHONY PAUL (US); PFIZER (US)) 12 November 1998 (1998-11-12) claims 1,4,11	1,2
X	WO 00 23061 A (DEMOPULOS GREGORY A ; HERZ JEFFREY M (US); PALMER PAMELA P (US); OM) 27 April 2000 (2000-04-27) claims 1,3,14	1,2,11

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

8 July 2002

Date of mailing of the international search report

16/07/2002

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 01/00683

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-11 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-16
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-16

Present claims 1-16 relate to compounds and therapeutic applications defined (inter alia) by reference to the following parameters: "COX-2 selective inhibitor", "cardiovascular protective amount of a thromboxane inhibitor" and "COX-2 mediated conditions".

The use of these parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to combinations of the COX-2 selective inhibitors individually structurally identified by name in the claims and the thromboxane inhibitors individually structurally identified by name on page 16 and 17 of the description, with due regard to the specified therapeutic applications mentioned in the claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 01/00683

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9850033	A	12-11-1998	AU 6932198 A	27-11-1998
			BG 103852 A	30-06-2000
			BR 9808720 A	11-07-2000
			CN 1255059 T	31-05-2000
			EP 0988034 A1	29-03-2000
			HR 980244 A1	28-02-1999
			HU 0001286 A2	28-11-2000
			WO 9850033 A1	12-11-1998
			JP 2000513020 T	03-10-2000
			NO 995389 A	04-01-2000
			NZ 500183 A	26-04-2002
			PL 337003 A1	31-07-2000
			SK 148199 A3	11-09-2001
			ZA 9803722 A	04-11-1999
WO 0023061	A	27-04-2000	AU 1214800 A	08-05-2000
			WO 0023061 A2	27-04-2000
			US 2002028798 A1	07-03-2002